REMARKS

Claims 1-21 remain before the Examiner for reconsideration. Claims 1, 6, and 15 are currently amended.

In the Office Action dated February 26, 2004, the Examiner rejected Claims 1-11 under 35 U.S.C. 112, first paragraph, "as failing to comply with the written description requirement." Specifically, the Examiner asserted that:

> The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no explanation in the specification nor the disclosure supports [sic] for the added limitation 'controlling at least one parameter during preparation of the medium'. The disclosure mentions about controlling parameters during delivery but does not mention about controlling parameters during preparation of the medium.

Applicants respectfully traverse the Examiner's rejection.

For example, in the third full paragraph on page 6, of the specification, Applicants set forth that:

> In a preferred embodiment, the sensor measures the properties of the contrast enhancement agents to control the preparation of the medium, the delivery of the medium and/or an imaging procedure carried out in conjunction with delivery of the medium.

Emphasis added. Likewise, in the second full paragraph on page 9 of the specification, Applicants set forth that:

> Further, the present invention provides a method of preparing a medium with contrast enhancement agents therein. The method comprises the step of measuring the concentration or other property of the contrast enhancement agents during preparation of the medium to assist in properly preparing the medium. Likewise, the present invention provides a system for preparing a contrast medium with contrast enhancement agents therein comprising a mixing container, an agitation mechanism for agitating the contents of the mixing container and a sensor adapted to measure the

> concentration or other property of the contrast enhancement agents in the container.

The specification of the present invention thus provides clear support for controlling at least one parameter (of preparation) during preparation of the a medium with contrast enhancement agents therein based upon a measured property (for example, concentration or size distribution) of the contrast enhancement agents during the preparation.

The Examiner also maintained the rejection of claims 1, 6-8, 12, 15, 16, 20, and 21 under the judicially created doctrine of obviousness-type double patenting "as being unpatentable over claims 44 (regarding claim 1), 70 (regarding claims 6-8), 39 (regarding claims 12, 15, 16), and 25 (regarding claims 20, 21) of U.S. Patent No. 6,317,623."

Specifically the Examiner asserted that:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because it is obvious to an ordinary skill in the art that concentration is a property of a contrast enhancement agent. Furthermore, the claims of the instant application is broader in scope than the claims of the `623 patent.

In response to Applicants' arguments set forth in the Amendment files June 28, 2004, the Examiner further asserted that:

> In regard to the double patenting rejection, examiner agrees that the instant application is a divisional application but it is not clear how the pending claims appear in the issued patent (US 6,317,623). A divisional case should not include any claims that are already examined in the parent case. Therefore, the examiner maintains the double patenting rejection.

Applicants respectfully traverse the Examiner's rejection.

As recognized by the Examiner, the present patent application is a divisional application filed as a result of a restriction requirement during the prosecution of U.S. Patent No. 6,317,623. Applicants thus once again respectfully assert that the Examiner's assertion of double patenting over U.S. Patent No. 6,317,623 is improper as 35 U.S.C. Section 121 sets forth that "a patent issuing on an application with respect to which a requirement for restriction under this section has been made ... shall not be used as a

reference either in the Patent and Trademark Office or in the courts against a divisional application...." In other words, as set forth in Section 804 of the MPEP:

> Generally, a double patenting rejection is not permitted where the claimed subject matter is presented in a divisional application as a result of a restriction requirement made in a parent application under 35 U.S.C. 121.

Applicants thus respectfully request that the Examiner withdraw the double patent rejection.

The Examiner also rejected Claims 1-5 and 15-19 under 35 U.S.C. 102(b) "as being anticipated by Giddey et al. (US 5,310,540)." Specifically the Examiner asserted that:

> Giddey teaches in col. 10, lines 13-37, a method of preparing contrast agents (gas-filled microspheres) comprising the step measuring the concentration or size of the contrast agents in order to assist in properly preparing the contrast agents. Giddey further teaches the pressurizing and agitating steps (col. 9, lines 22-39). Giddey continues to teach the steps controlling the size distribution and concentration of the contrast agents (col. 9, line 36 and col. 11, line 54). Giddey's contrast agent is used for ultrasonic diagnostic imaging system which inherently suggests the step of imaging a patient.

In response to the Applicants' argument set forth in the Amendment filed June 28, 2004, the Examiner further asserted that:

> With respect to the patentable subject matter, the applicant's core argument is that the prior arts of record (as applied in the prior office action) alone or in combination teaches or suggests measuring a property of the contrast agents during preparation or delivery., The examiner respectfully disagrees. Giddey teaches in col. 10, lines 13-37, a method of preparing contrast agents (gas-filled microspheres) comprising the step measuring the concentration or size of the contrast agents in order to assist in properly preparing the contrast agents.

Applicants respectfully traverse the Examiner's rejection.

Once again, Giddey discloses whipping a viscous solution of a filmogenic protein into a foam and subjecting the foam to shear to reduce the size of the foam bubbles to a

range suitable for use in ultrasonic echography. Giddey, in column 9, lines 22-39, merely describes a series of experiments in which various parameters were changed between experiments and certain properties of the resultant preparation (after the preparation thereof) were measured and recorded. Giddey does not disclose or suggest measuring a property of the contrast enhancement agents during preparation of the medium and controlling at least one parameter (of the preparation) during the preparation of the medium at least in part based upon the measured property. Applicants have amended claim 1 to more clearly set forth the present invention.

Likewise, Giddey does not disclose or suggest a method of delivering a medium with contrast enhancement agents therein to a patient during an injection procedure, including: measuring a property of the contrast enhancement agents during delivery to the patient during the injection procedure; and selectively destroying one or more of the contrast enhancement agents to control the measured property. Indeed, Giddey discloses a method for the initial preparation of a contrast medium by a manufacture thereof and does not address issues related to controlling the preparation of a contrast medium including contrast enhancement agent therein during an injection procedure in which the contrast medium is delivered to a patient.

The Examiner further Claims 1, 5, 15, 18, and 19 under 35 U.S.C. 102(b) "as being anticipated by Cheung (US 5,194,300) or Guberek et al. (US 5,230,343) or Orsolini et al. (US 5,445,832)." Specifically the Examiner asserted that:

> Cheung teaches in col. 5, lines 4-54 or Guberek teaches in col. 5, lines 5-25 or Orsolini teaches in col. 4, lines 26-35, a method of preparing contrast agents comprising the step of measuring the size of the contrast agents.

In response to the arguments set forth by Applicants in the Amendment filed June 28, 2004, the Examiner merely repeated that:

> Cheung teaches in col. 5, lines 4-54 or Guberek teaches in col. 5, lines 5-25 or Orsolini teaches in col. 4, lines 26-35, a method of preparing contrast agents comprising the step of measuring the size of the contrast agents.

Applicants respectfully traverse the Examiner's rejection.

Cheung discloses highly fluorescent latex microspheres and preparation thereof. The microspheres can be used to visualize cell surface antigens and DNA encoding of single genes via a biotinylated DNA probe. In that regard, the microshperes of Cheung are used in fluorescence microscopy and flow cytometry procedures to detect feartures of substrates to which the microspheres are attached. The fluorescent markers of Cheung are not contrast enhancement agents and are not used in patient imaging. Indeed, Cheung is not analogous art to the present invention and is irrelevant to the present invention. In any event, Cheung does not disclose or suggest measuring a property of the contrast enhancement agents during preparation of the medium and controlling at least one parameter (of the preparation) during the preparation of the medium at least in part based upon the measured property. Likewise, Cheung does not disclose or suggest a method of delivering a medium with contrast enhancement agents therein to a patient during an injection procedure, including: measuring a property of the contrast enhancement agents during delivery to the patient during the injection procedure; and selectively destroying one or more of the contrast enhancement agents to control the measured property. Chueng, at Column 5, lines 4-54, merely discloses the method of preparation of the fluorescent latex microshperes thereof wherein the properties of the microspheres are measured after preparation.

Guberek discloses the measurement and tracing of regional myocardial blood flow and other blood flows using nonradioactive, colored microspheres. The colored microspheres of Guberek are not contrast enhancement agents used in patient imaging. Like Cheung, Guberek is not analogous art to the present invention. Moreover, Guberek does not disclose or suggest measuring a property of the contrast enhancement agents during preparation of the medium and controlling at least one parameter (of the preparation) during the preparation of the medium at least in part based upon the measured property. Likewise, Guberek does not disclose or suggest a method of delivering a medium with contrast enhancement agents therein to a patient during an injection procedure, including: measuring a property of the contrast enhancement agents

during delivery to the patient during the injection procedure; and selectively destroying one or more of the contrast enhancement agents to control the measured property. Guberek, at Column 5, lines 5-25, merely discloses the introduction of the already-prepared colored microshperes into the flow and subsequent analysis after recovery of a sample of the volume.

Orsilini et al. discloses the preparation and use of microspheres of a biodegradable polymer material incorporating a medicamentous substance for sustained and controlled release of the medicamentous substance. Orsilini et al. does not disclose or suggest a contrast medium including contrast enhancement agents therein for use in patient imaging. Like Chueng and Guberek, Orsilini et al. is not analogous art for the present invention. Furthermore, Orsilini et al. does not disclose or suggest measuring a property of the contrast enhancement agents during preparation of the medium and controlling at least one parameter (of the preparation) during the preparation of the medium at least in part based upon the measured property. Likewise, Orsilini et al. does not disclose or suggest a method of delivering a medium with contrast enhancement agents therein to a patient during an injection procedure, including: measuring a property of the contrast enhancement agents during delivery to the patient during the injection procedure; and selectively destroying one or more of the contrast enhancement agents to control the measured property. Orsolini et al., at Column 4, lines 26-35, merely discloses that the method of preparation of that invention enables control of size of the medicamentous-substance-containing microspheres produced thereby.

The Examiner also rejected Claims 6 and 10 under 35 U.S.C. 103(a) "as being unpatentable over Evans, III et al. (US 5,885,216) in view of Giddey et al.". Specifically the Examiner assured that:

> Evans teaches a container (10) and a sensor adapted to measure concentration of the contrast agent but fails to mention specifically an agitation mechanism.
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> Giddey teaches in col. 9, lines 17-35, an agitation mechanism specifically used in preparation of ultrasonic contrast agents in order to agitate the

> contrast agents so that intended concentration of the contrast agents is achieved.
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> Therefore, it would have been obvious to an ordinary skill in the art at the time the invention was made to use the agitation mechanism of Giddey in the contrast agent preparation process of Evans so that intended concentration of the contrast agents is achieved.

Applicants respectfully traverse the Examiner's rejection.

Evans discloses use of a bulk container of a contrast medium and a bulk container of a diluent (for example, saline) to deliver contrast medium of a desired concentration to a plurality of patients wherein a contamination prevention means is provided to eliminate cross-contamination between patients. Evans further discloses a preferred methodology of manual insertion of data regarding contrast concentration or use of a sensor which reads a bar code on a contrast container (which can include information regarding the concentration of the contrast medium). As also set forth in Evans, a backup sensor can be employed to provide assurance:

> In the present disclosure, all embodiments employ an electronic control system which provides the proper fluid flows according to the instructions of the operator. The operator can either input information on the concentrations in the various containers, or the control system can read a bar code or other code on the bulk container which informs it of the volume and concentration in that bulk container. Also, there can be sensors which inform the control system when a bulk container empties, or the control system can keep track of the volume removed and anticipate when it will run out. Anticipation is preferred because an operator can then be informed during programming of the need to add fluid, rather than start a procedure and then run out.
>
> There is a benefit to having back-up monitors for these important parameters. If the system anticipates when fluid runs out, there can still be fluid assurance sensors, in case a technician installs a partially used bottle. Especially when the contrast is being delivered to a patient, there needs to be a fluid assurance sensor to prevent the problem of air embolism. While concentration is not as critical, an improper concentration can necessitate repeat procedure. A sensor measuring electro-conductivity could be used for both concentration monitoring and fluid assurance. There are commercially available ultrasonic sensors designed to detect the presence or absence of fluid in a line. For example, U.S. Pat. No. 4,981,467 discloses such a detector.

Col. 3, line 57 to Col. 4, line 35. However, Evans does not disclose or suggest a system for preparing a medium with contrast enhancement agents therein comprising: a container including the medium; an agitation mechanism operably associated with the container for agitating the medium; a sensor adapted to measure a property of the contrast enhancement agents in the container; and a controller operable to control a parameter of the preparation of the medium during preparation of the medium at least in part in on the basis of the measured property. As admitted by the Examiner, Evans doew not disclose or suggest an agitation mechanism operably associated with a container including a contrast medium. Moreover, there is no motivation provided in Evans or Giddey for such a combination. See, for example, *Ex parte* Chicago Rawhide Mfg. Co., 223 USPQ 351, 353 (P.O. Bd. Appl. 1984) ("The prior art must provide a motivation or reason for a worker in the art without the benefit of appellant's specification to make the necessary changes in the reference device."); Schenk v. Norton, 218 USPQ 698, 702 (Fed. Cir. 1983) ("Modification unwarranted by the disclosure of a reference is improper."); Ex Parte Acosta, 211 USPQ 636, 637 (P.O. Bd. Appls. 1980) (Examiner's combination of two references is improper where there is no basis in the record from which it can reasonably be inferred that one skilled in the art would have been led or motivated to modify the primary reference in the manner proposed by the Examiner.). In any event, mere addition of an agitating element to the system of Evans would not result in the present invention as set forth in claims 6 and 10. For example, there is no disclosure or suggestion in Evans or Giddey (or any combination thereof) of a controller operable to control a parameter of the preparation of the medium during preparation of the medium at least in part in on the basis of the measured property. For this reason and for the reasons set forth above, the disclosure of Evans cannot be combined with the disclosure of Giddey to render the present invention obvious.

Finally, the Examiner objected claims 9 and 11 "as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims." In view of the amendment and remarks set forth above, Applicants respectfully assert that claims 9 and 11 are allowable.

In view of the above amendments and remarks, the applicants respectfully requests that the Examiner withdraw the objection to the drawings and the rejections of the claims, indicate the allowability of Claims 1-21 rand arrange for an official Notice of Allowance to be issued in due course.

Respectfully submitted,

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